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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

EXAMINER

MEHTA, ASHWIN D

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1638

DATE MAILED: 11/19/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/845,849

Applicant(s)

WEIGEL ET AL.

Examiner

Ashwin Mehta

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 September 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-34 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-24, 28, 29, 33 and 34 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 25-27 and 30-32 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 30 April 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, claims 1-24, 28, 29, 33, and 34 in Paper No. 8, received 05 September 2002, is acknowledged. Non-elected claims 2-27, 30-32, and 34 are withdrawn from consideration and require cancellation.

Priority

2. The priority statement, submitted in the preliminary amendment received 04 September 2001, should be changed. Instead of indicating that the instant application claims the benefit of priority from Application Serial No. 09/060,726, it should indicate the relationship to the parent application. It is suggested that "claims the benefit of priority from" be changed to --is a divisional of--.

Specification

3. The specification is objected to because it fails to comply with the sequences rules of 37 CFR 1.821-1.825. The amino acid sequences in Figures 2, 3A, and 3C should be identified in the brief descriptions of those figures by their sequence identifiers.

4. The paragraph on lines 20-24 on page 7 contains markings, the presence of which does not appear to be intentional. The handwritten correction appears in the sentence spanning lines

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9-11 on page 8. It is suggested that these paragraphs be replaced, so that these markings are removed. New matter must be avoided.

Claim Objections

5. Claims 2-5, 18, and 20 are objected to for the following minor informalities:

In claims 2 and 20: the claims are missing the period punctuation mark.

In claims 3-5: the recitation "NOS:3" in line 2 of the claims should read --NO: 3--.

In claim 18: the term --at-- should be inserted before "least" in line 1.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-18, 21, 28, 29, 33, and 34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1-6, 17, and 18: the recitation "antisense FT-encoding nucleotide sequence" renders the claims indefinite. The recitation suggests that the sequence actually encodes an FT protein, which it cannot since it is complementary to the sequence that does.

In claim 8: the claim recites the recitation "the structural gene" in line 1. There is insufficient antecedent basis for this limitation in the claim or the claim from which it depends.

In claim 12: the claim recites the recitation "the nucleic acid" in line 1. There is insufficient antecedent basis for this limitation in the claim or the claim from which it depends.

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In claims 15 and 16: the claims are drawn to either a plant cell or plant tissue of the plant of claim 1. However, it is not clear if the cell or tissue comprises the exogenous antisense FT-encoding nucleotide sequence in its genome.

In claims 18 and 20: the recitation "the least one exogenous antisense FT-encoding nucleotide sequence has at least 80% sequence homology to SEQ ID NO: 3" renders the claim indefinite. It is not clear if the claims are limiting the seed or vector to comprise just one antisense sequence that has at least 80% homology to SEQ ID NO: 3, or if there is more than one antisense sequence, all of which have at least 80% homology to SEQ ID NO: 3.

In claim 21: the recitation "the vector comprises a T-DNA derived vector" renders the claim indefinite. The recitation indicates that a vector has another vector within it. It is suggested that the term "comprises" be replaced with --is--. The recitation "T-DNA derived vector" also renders the claim indefinite. It is not clear what is meant by "derived." It is suggested that "derived" be deleted.

In claim 28, 33, and 34: the claims are indefinite for being dependent on non-elected claims.

In claim 29: the recitation "comprises has at least". It is not clear what is meant by this recitation.

In claim 34: the claims limits the structural gene to have 80% sequence homology to SEQ ID NO: 3. However, SEQ ID NO: 3 is an antisense sequence, and is not itself a structural gene.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1, 7-17, 19, 21-24, 33, and 34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn towards any genetically modified plant comprising at least one exogenous antisense FT-encoding nucleotide sequence in its genome and having the phenotype of delayed flowering; or wherein said plant further comprises any dominant negative mutation in a nucleotide sequence encoding a polypeptide selected from the group consisting of: LFY, AP1, CO, FLO, SQUA, FCA, and any combination thereof; any plant cell or tissue derived from said plant; any seed which germinates into said plant; any vector containing a nucleotide sequence comprising at least one antisense FT sequence that inhibits flower development, operably associated with a promoter; or wherein said vector further comprises an exogenous gene encoding any dominant negative mutation in a nucleotide sequence encoding a polypeptide selected from the group consisting of: LFY, AP1, CO, FLO, SQUA, FCA, and any combination thereof; or a method of producing a genetically modified plant comprising contacting a plant cell with a vector comprising any nucleotide sequence comprising at least any structural gene disrupting or interfering with expression of any flowering time gene, wherein the structural gene is in antisense orientation.

The specification describes the isolation and sequencing of a cDNA encoding the Flowering Locus T (FT) protein of Arabidopsis (Examples 1 and 2, pages 38-41). The

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specification indicates that functional information was available for a pair of orthologous genes in plant, and another pair on mammals. Inactivation of the plant orthologs, CEN from snapdragon and TFL1 from Arabidopsis, causes the formation of terminal flowers. tfl1 mutants further flower slightly earlier than wild type, and TFL1, while related in sequence to the Arabidopsis FT, has an opposite role in flowering (page 39, lines 9-21). The specification indicates that the N-terminus of the mammalian orthologous proteins, when cleaved from the protein, is an active principle in stimulating acetylcholine synthesis, and that based on sequence alignment, the minimum consensus sequence was deduced to be X-Gly-Pro-Leu. The specification indicates that while the amino termini of the plant proteins are diverged, all share the sequence (Asp or Glu)-Pro-Leu (page 40, line 10 to page 41, line 9). The specification also indicates that the Arabidopsis FT-encoding nucleotide sequence was operably linked to the CaMV 35S promoter in sense (SEQ ID NO: 5) or antisense (SEQ ID NO: 3) orientation and expressed in transgenic Arabidopsis plants. Plants expressing the sense construct flowered earlier than wild type, and plants expressing the antisense construct flowered late (Example 3, pages 41-42).

However, the specification does not teach the antisense sequence of any other FT-encoding nucleotide sequence other than SEQ ID NO: 5. The specification does not describe the nucleotide sequences that encode any other FT protein. As discussed above, the specification indicates that the Arabidopsis FT encoded by SEQ ID NO: 5 has a consensus sequence at its N-terminus, and that the other proteins listed in Figure 3C, which include the snapdragon CEN and the Arabidopsis TFL1, also contain this consensus sequence (page 41, lines 3-9). However, as discussed above, CEN and TFL1 do not share the same functional activity as FT. Therefore, the

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structure of this consensus sequence is not specifically correlated with the activity of FT. The specification does not teach any other functional domains, such as catalytic domains, binding sites, etc., that are important for FT function. One skilled in the art then cannot correlate the structure of other FT-encoding nucleotide sequences with function, and therefore their antisense sequences are also not described.

The specification also does not teach the sequences of any dominant negative mutations of the nucleotide sequences encoding the proteins listed in claims 7 and 22. No information is described at all concerning any mutations of these sequences that would make them dominant negatives. See *University of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997), where it states: "The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA... Accordingly, the specification does not provide a written description of the invention..." Also see *Fiers* 25 USPQ 2d (CAFC 1993) at 1606, which states that "[a]n adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself". Given the breadth of the claims encompassing any antisense FT-encoding nucleotide sequence, any dominant negative mutation encoding the proteins mentioned in claims 7 and 22, and lack of guidance as discussed above, the specification fails to provide an adequate written description of the multitude of nucleotide sequences encompassed by the claims.

8. Claims 1-5, 7-24, 28, 29, 33, and 34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a genetically modified plant with delayed flowering comprising SEQ ID NO: 3, does not reasonably provide enablement for genetically modified plants, or methods of making said plants, with delayed flowering comprising the antisense sequence of any other FT-encoding nucleotide sequence, sequences encoding at least 80%, 85%, 90%, 95% sequence homology to SEQ ID NO: 3, dominant negative mutations of LFY, AP1, CO, FLO, SQUA, or FCA. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are broadly drawn towards any genetically modified plant comprising at least one exogenous antisense FT-encoding nucleotide sequence in its genome and having the phenotype of delayed flowering; or wherein the antisense exogenous FT-encoding nucleotide sequence has at least 80%, 85%, 90%, or 95% homology to SEQ ID NO: 3; or wherein said plant further comprises any dominant negative mutation in a nucleotide sequence encoding a polypeptide selected from the group consisting of: LFY, AP1, CO, FLO, SQUA, FCA, and any combination thereof; any plant cell or tissue derived from said plant; any seed which germinates into said plant; any vector containing a nucleotide sequence comprising at least one antisense FT sequence that inhibits flower development, operably associated with a promoter; or wherein said vector further comprises an exogenous gene encoding any dominant negative mutation in a nucleotide sequence encoding a polypeptide selected from the group consisting of: LFY, AP1, CO, FLO, SQUA, FCA, and any combination thereof; or a method of producing a genetically

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modified plant comprising contacting a plant cell with a vector comprising any nucleotide sequence comprising at least any structural gene disrupting or interfering with expression of any flowering time gene, wherein the structural gene is in antisense orientation; or a method for genetically modifying a plant cell such that the plant produced from it has delayed flowering, comprising introducing any antisense FT nucleotide sequence in the plant, or wherein said antisense FT nucleotide sequence comprises at least 85% homology to SEQ ID NO: 3.

As discussed above, the specification teaches the nucleotide sequence (SEQ ID NO: 5) encoding an Arabidopsis FT protein, and its antisense sequence (SEQ ID NO: 3). The specification teaches that transgenic plants expressing SEQ ID NO: 5 exhibit accelerated flowering time, and plant expressing SEQ ID NO: 3 exhibit a delay in flowering. However the specification does not teach any other FT-encoding nucleotide sequence besides SEQ ID NO: 5, and therefore their antisense sequences. No other FT-encoding nucleotide sequences and their antisense sequences have been reduced. See In re Bell, 26 USPQ2d 1529, 1532 (Fed. Cir. 1993) and In re Deuel, 34 USPQ2d, 1210 (Fed. Cir. 1995), which teach that the mere existence of a protein does not enable claims drawn to a nucleic acid encoding that protein. See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016 at 1021 and 1027, (Fed. Cir. 1991) at page 1021, where it is taught that a gene is not reduced to practice until the inventor can define it by “its physical or chemical properties” (e.g. a DNA sequence).

The specification also does not teach that any nucleotide sequence that has at least 80%, 85%, 90%, or 95% sequence homology with SEQ ID NO: 3 caused a delay in flowering time in any genetically modified plant. Branch discusses how scientists have sought to use antisense sequences to block the expression of selected genes, but have caused unwanted effects due to, for

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example, an effect of the antisense molecule on unintended targets. Branch also discusses how target RNAs often create physical barriers that render potential binding sites inaccessible (pages 45-49). It then cannot be predicted that sequences that differ from SEQ ID NO: 3 will cause the same effect when expressed in a transgenic plant. It would require undue experimentation by one skilled in the art to determine how SEQ ID NO: 3 can differ, and still cause a delay flowering time when expressed in a transgenic plant.

Further, the specification does not teach any dominant negative mutations of any of the nucleotide sequences mentioned in the claims. The specification does not provide any guidance at all as to one would produce any such dominant negative mutants. In the absence of further guidance, undue experimentation would be required by one skilled to determine how the sequences encoding the proteins mentioned in the claims should be changed such that a dominant negative mutant is produced. See Genentech, Inc. V. Novo Nordisk, A/S, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997), which teaches that “the specification, not the knowledge of one skilled in the art” must supply the enabling aspects of the invention.

Furthermore, it is not clear how one would use the plants encompassed by claim 7. For example, Irish et al. (Plant Cell, 1990, Vol. 2, pages 741-753) teach that AP1 mutant plants display a homeotic conversion of sepals into bracts, the concomitant formation of floral buds in the axil of each transformed sepal, and that flowers lack petals (pages 742-745). It is not clear, and the specification does not teach, how one would use the claimed plant that expresses any antisense FT-encoding nucleotide sequences and a dominant negative mutant AP1 that is delayed in the flowering of abnormal flowers, if this is even the phenotype that one would obtain. The

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specification does not teach the phenotype of any of the double mutant plants, nor how one would use them. See Genentech, Inc. V. Novo Nordisk, A/S, supra.

Further regarding claims 33 and 34: the claims indicate that the antisense sequence of a structural gene, that disrupts or interferes with the expression of any flowering time protein, is to be expressed. It is not clear how one skilled in the art can use such an antisense sequence to block the flowering time protein, when the intended target of the antisense sequence would be structural gene. Given the breadth of the claims encompassing the genetically modified plants comprising the antisense sequence of any FT-encoding nucleotide sequence, or sequences having least 80% to at least 95% homology with SEQ ID NO: 3, and wherein said plants have dominant negative mutations in other flowering genes listed in the claims, unpredictability of the art and lack of guidance of the specification as discussed above, undue experimentation would be required by one skilled in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

9. Claim 33 is rejected under 35 U.S.C. 102(a) as being anticipated by Song et al. (Plant Physiol., 1997, Vol. 114, pages 927-935)

The claim is broadly drawn towards a method of producing a genetically modified plant comprising contacting a plant cell with a vector comprising a nucleotide sequence comprising at

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least a structural gene disrupting or interfering with expression of any flowering time gene encoded polypeptide, wherein the structural gene is in an antisense orientation, to obtain a transformed plant cell and producing and selecting a plant that exhibits late flower development relative to a wild type plant.

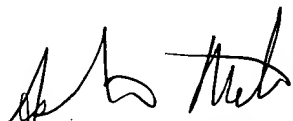
Song et al. teach the production of transgenic Arabidopsis plants expressing the antisense sequence of the AtPTR2-B gene. Plasmids comprising the antisense sequence were introduced into root-explants via Agrobacterium transformation, and transgenic plants were regenerated. The transgenic plants exhibited delayed flowering (pages 928-931).

10. Claims 1-24, 28, 29, 33, and 34 are rejected.

Contact Information

Any inquiry concerning this or earlier communications from the examiner should be directed to Ashwin Mehta, whose telephone number is 703-306-4540. The examiner can normally be reached on Mondays-Thursdays and alternate Fridays from 8:00 A.M to 5:30 P.M. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at 703-306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 and 703-872-9306 for regular communications and 703-872-9307 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

November 16, 2002


ASHWIN D. MEHTA, PH.D.
PATENT EXAMINER